



innate pharma

# NEWSLETTER TO #8 november 2010 SHAREHOLDERS

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## EDITORIAL

### Dear Shareholders,

As we mentioned during the December 2009 fund-raising process and at the full year results publication in March, our roadmap for the next two years is fairly simple: move on the clinical programme for the anti-KIR approach, look for new industrial partners and reinforce our preclinical portfolio of antibody drug candidates. These three objectives have been outlined and followed with the commitment of each one of us, and we hope to see the results very soon. The recent news that a new IPH 2101 study has begun provides an opportunity to update you on the first objective, which is mobilizing a large part of the company’s resources.

Lastly, in the i<sup>2</sup> section, we want to come back on major news in cancer immunotherapy which were published in 2010 and are producing a positive perception of this approach by the physicians and the industry. We also invite you to hear to scientists, physicians and industrials who met during a round table a few months ago to take stock of this innovative approach. As you will see, after more than 30 years of research and development, punctuated by as many breakthroughs as attempts and disappointments, we are surely on the brink of seeing the development of new immunotherapy approaches in oncology. Through its scientific choices, Innate Pharma is set to be a major player in this new era.

We also take advantage of this letter to review the changes announced last June in the Supervisory and the Executive Boards, but also the ones, less visible from the outside, realized in the operational teams.

We hope that, like previous letters, this one will enable you to share our sense of purpose and our confidence, and assure you that our commitment to these projects is unwavering.

The Company is indeed forging ahead, the better to carry out its mission: developing innovative antibodies to treat cancer and inflammation by acting on the innate immunity system.

Wishing you an excellent read,

**HERVÉ BRAILLY,**  
Chairman of the Executive Board  
Chief Executive Officer

### UPCOMING CONFERENCES

Annual meeting of the French Society for Immunology (SFI) November 24-26, 2010, Marseilles, France

Annual meeting of the American Society of Hematology (ASH) December 4-7, 2010, Orlando, FL, USA

Healthcare & Biotechnology Conference, organized by Société Générale on February 9, 2011, Paris, France

Smallcap Event of Paris April 25 and 26, 2011, Paris, France



## Changes in the Supervisory Board and the Management team

At the last Shareholders' General Meeting, the Supervisory Board welcomed Patrick Langlois, previously Group Executive Vice-President and CFO of Aventis.

The Company also said goodbye to Stéphane Boissel, Executive Vice-President and CFO since 2002 and Hemanshu Shah, CBO since 2008. The Company is now looking for a new CFO. Yannis Morel was appointed Senior Director, Business Development and will replace Hemanshu Shah. Marcel Rozenzweig, Executive Vice-President, Medical and Regulatory Affairs, was appointed CMO of the Company.

At the operational level, the "Development" teams have been reinforced notably to carry through with the IPH 2101 clinical program. Today, more than 20 people are working on trial management, medical strategy, regulatory affairs, pharmacovigilance, quality control, pharmaceutical operations, etc.

In "Research", the Company's new positioning has led to the strengthening of the antibody platform. This platform is dedicated to validating new target, generating and optimizing antibodies and demonstrating proof-of-concept in several efficacy models. Two pharmacology teams also participate to these projects and a transversal group was set to spot and pre-evaluate new targets. All in all, more than 30 people are implied in the Research works.

Half of the people dedicated to Research and Development are doctors (PhD., MD., PharmD.).



### Interview with Patrick Langlois

#### Could you tell us about your appointment to the Innate Pharma Supervisory Board?

I was appointed on recommendation from the FSI (the French sovereign fund). I accepted the job with great pleasure and enthusiasm: since having left the corporate world, Aventis, I have developed a passion for entrepreneurial ventures with the potential to become the success stories of tomorrow.

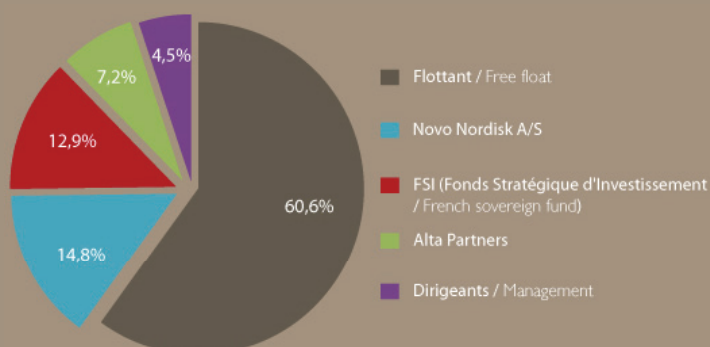
I wholeheartedly share the conviction which triggered the FSI investment that Innate Pharma has a unique and promising position within the European biotech companies. The company is currently undergoing critical changes to become a major player in the development of antibodies to fight cancer and inflammation. I am convinced of the relevance of Innate's projects, while remaining aware of the risks associated with such research & development.

#### What can you contribute to Innate?

My career with Aventis makes me particularly suited to work in corporate finance, market communications and agreements. I therefore hope to be able to advise Innate the best I can in these fields, as well as on overall strategic aspects. I have been working for the company for 6 months now and I can say that, having met the teams several times, I am very impressed with their level of skills and capacity to carry through with so many projects.

## SHARE INFORMATION

### SHAREHOLDING STRUCTURE, 4Q 2010



### STOCK MARKET INFORMATION

Mnemo: IPH / ISIN Code: FR0010331421

Stock Market: NYSE Euronext Paris Eurolist (compartment C)

Total number of outstanding shares: 37,686,794

### ANALYSTS

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### UPCOMING EVENT IN OUR FINANCIAL CALENDAR FOR 2010: February 4, 2011

Publication of revenue for 4Q2010 and for fiscal year 2010, with management comments

### INVESTOR RELATIONS

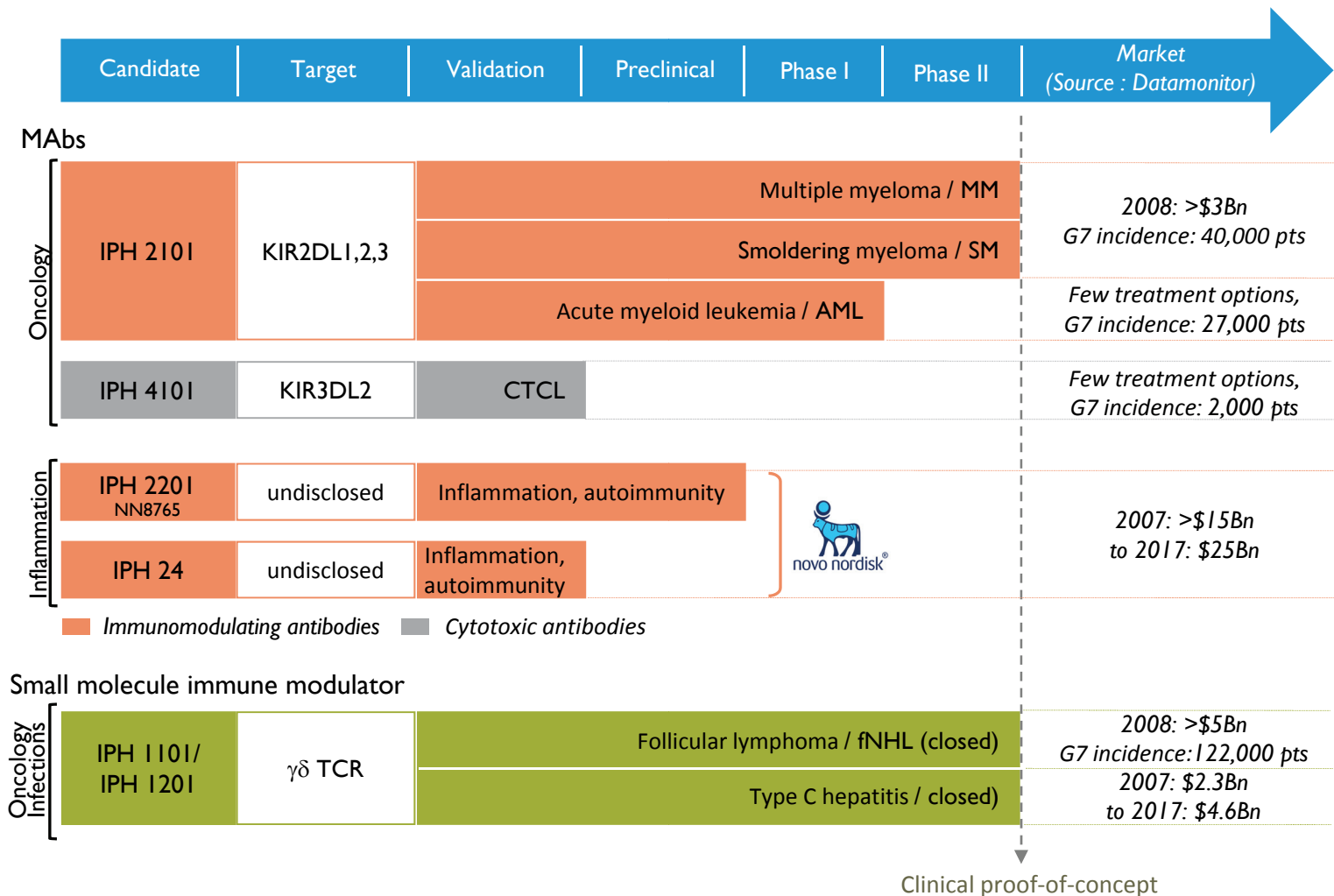
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## Product pipeline as at 4Q 2010



### IPH 1101: Completion of the Phase II program

Last June, Innate Pharma announced the final results on the response rate for the IPH 1101-202 study. This completes the Phase II program of its first historical candidate, IPH 1101. This small molecule activates gamma delta T cells, lymphocytes (white blood cells) which are able to kill cancer cells as well as to produce chemical messengers to induce a global inflammatory response.

The IPH 1101 Phase II program comprised four trials; three in cancer and one in an infectious indication, type C hepatitis ("HCV"). It began in 2006 and delivered results from 2008 to 2010. Two trials showed the clinical activity of IPH 1101: the HCV trial (results were reported in June 2009) and the follicular lymphoma trial, where IPH 1101 was tested in combination with rituximab (results were reported in June 2010).

Innate Pharma is currently looking for a partner to further develop this program as the next steps would include randomized trials, thus implying logistical and financial capacities beyond Innate's own capacities. It is also a turning point for the Company since it will now focus solely on developing monoclonal antibodies as drug candidates.

### IPH 2101: Phase II program set-up

The initiation of a new Phase II clinical trial with IPH 2101 is an opportunity to update the global clinical program. Three Phase II trials are testing the drug candidate in different settings in Myeloma patients:

- Response maintenance/ consolidation, single agent
- Relapse, in combination with lenalidomide
- Smoldering myeloma, single agent

*More information on the next page*



### IPH 2101 Phase II program: testing different settings in multiple myeloma patients

- **Response maintenance/ consolidation, single agent**

IPH 2101 is being tested in multiple myeloma patients who have partially responded to a first line of treatment. This trial started in 2009 and is looking to enhance the response with IPH 2101. This positioning is very close to the post-bone-marrow transplantation setting for which we have strong, though indirect, clinical-proof-of-concept data ([see the IPH 2101 section on the Company's website](#)).

- **Relapse, in combination with lenalidomide (Revlimid®, Celgene Corporation)**

The combination is being tested in patients who responded to a first line of treatment and then relapsed. NK cell activation is one of the mechanisms of action of lenalidomide. We therefore hope to show synergy between both products. Innate Pharma and Celgene collaborate to this study, which should begin recruiting patients in the coming weeks.

- **Smoldering myeloma, single agent**

This stage of the disease is asymptomatic and characterized by the presence of very few tumor cells. It can evolve in an active myeloma with a 10% risk per year in the first five years. Patients are currently not treated for this condition notably because there is no well-tolerated therapy available. There is therefore a strong rationale to test the anti-KIR approach in this indication: favorable tumor cells/ NK cells ratio and demonstration of a very good safety for IPH 2101 in clinical trials.

IPH 2101 is being tested in multiple myeloma (“MM”) and acute myeloid leukemia (“AML”), two NK-sensitive indications. Unlike acute myeloid leukaemia, multiple myeloma benefits from a surrogate marker that makes it possible to rapidly monitor whether the product has an impact on the disease (the M-protein, produced by myeloma cells). It is therefore a favorable situation for a Phase II trial.

The endpoint followed in acute myeloid leukaemia today is the progression-free survival of patients, which is currently about 10 to 12 months in the population selected. Randomized trials would be necessary to demonstrate an improvement in this duration, but would be a long process. Innate has thus chosen to extend its Phase I trial to 12 additional patients who will receive several treatment cycles in order to document product safety as well as progression-free survival in these patients.

### Other trial with IPH 2101 sponsored by the National Cancer Institute

Another Phase II trial is about to begin recruiting patients. This trial is not sponsored by Innate Pharma but by the National Cancer Institute. The NCI is part of the NIH (National Institutes of Health under the U.S. Department of Health and Human Services). It coordinates the National Cancer Program, which conducts and supports research, training, health information dissemination, and other cancer-related programs.

It will not only test IPH 2101 in smoldering myeloma with another administration regimen, but also provide additional information on the dynamics of KIR receptor saturation and on molecular markers associated with a potential clinical response.

We are extremely excited by the fact that NCI has chosen to include the anti-KIR approach in its own testing program for new promising drugs!

### After IPH 2101, welcome to IPH 2102

Lastly, a Phase I clinical trial with IPH 2102 will be shortly initiated. IPH 2102 is a second anti-KIR monoclonal antibody, targeting the same receptor as IPH 2101 but produced in another cell line (CHO instead of hybridoma). This shift will optimise the productivity and the product quality for commercial-scale production, a classical optimisation of the industrial process of antibody production.

IPH 2102 will be the drug candidate tested in registration trials.





## Summary of the clinical program for IPH 21 and upcoming newsflow

<p><b>Phase I in AML</b> France (one treatment cycle)</p>	<p>Phase I results were presented at the 2009 ASH meeting. This study was extended to recruit 12 additional patients who will receive several treatment cycles. Results for this additional cohort are expected in 2012.</p>
<p><b>Phase I in MM</b> USA (several treatment cycles)</p>	<p>Recruitment has been completed; seven patients were added to the last dose level, which brings the number of patients to 32. A poster will be presented at the upcoming ASH meeting in December. Final results of this study should be published in the second quarter of 2010.</p>
<p><b>Phase I with IPH 2102</b></p>	<p>First patient inclusion is expected in early 2011. Results are expected at the end of 2012.</p>
<p><b>REMIKIR</b> Phase II MM maintenance Single agent</p>	<p>42 patients. 2 arms with different dosage. Results (response rate on M protein level, safety, pharmacodynamics) are expected end of 2011 / beginning of 2012.</p>
<p><b>KIRIMID</b> Phase II MM relapse Combination with lenalidomide</p>	<p>33 patients. Results (response rate on M protein level, safety, pharmacodynamics) are expected end of 2012 / beginning of 2013.</p>
<p><b>KIRMONO</b> Phase II smoldering myeloma Single agent</p>	<p>30 patients. 2 arms with different dosage. Results (response rate on M protein level, safety, pharmacodynamics) are expected end of 2012 / beginning of 2013.</p>

## Interview with Marcel Rozenzweig, Executive Vice President and Chief Medical Officer



### *Could you tell us about the clinical trials for IPH 2101 that have been launched in the US?*

These major clinical trials should provide proof-of-concept for the anti-KIR approach in the above-mentioned indications, as well as validating NK cells as targets for therapeutic agents. They will also put us in touch with the main opinion leaders in hematologic cancer. In this respect, the US is just as important as Europe. We are feeling confident thanks to the manifest motivation of physicians. Our approach is not only appealing because clinical results demonstrate the sensitivity of myeloma and acute myeloid leukaemia to NK cells, but also because of the encouraging results obtained by other anti-cancer immunotherapies. This is highlighted by the fact that NCI has decided to test this approach. There are not that many innovative products currently being tested in this pathology by this prestigious institute!

### *What do you expect from the IPH 2101 Phase II clinical program?*

We will have results for the anti-KIR approach alone - this is important from a regulatory standpoint - but also in combination with lenalidomide, potentially the first combination of two immunologic approaches in this disease. Depending on the efficacy and safety results, these two strategies could be tested in the different settings described above, in registration studies. In acute myeloid leukaemia, we are considering a Phase II/III trial, to address the issue of obtaining an early anti-tumor signal within the framework of a randomized trial. We are still working on this issue.



### Interview with Marcel Rozenzweig (continued)

*You arrived at Innate in 2009. What conclusions would you draw from this experience after 18 months?*

I joined Innate because I was convinced of the originality and value of the Company's approach. However, I have to admit that the cancer immunotherapy sector was a bit sluggish. The last newsletter to Innate shareholders spoke of an encouraging trend observed at the last American Society of Hematology (ASH) annual meeting. I am pleased to say that this rather new and long-awaited trend has since been confirmed and has even become stronger. This was particularly felt at the last American Society of Clinical Oncology (ASCO) annual meeting, the most important international oncology conference of the year. Of the most impressive results that stood out during this event were those of ipilimumab for advanced melanoma.

Ipilimumab is an immunomodulating antibody developed in cancer and which exploits a very innovative mechanism of action. This antibody blocks an inhibitor receptor on the surface of some T lymphocytes to facilitate their activation. Does this sound familiar? IPH 2101 is an antibody that blocks an inhibitor receptor on the surface of NK cells - another type of lymphocyte!

The results of ipilimumab in melanoma are therefore very encouraging for us, even if they obviously cannot be directly extrapolated to IPH 2101. Such promising results for cancer immunotherapy do not stop here. In 2010, Provenge was approved for the treatment of prostate cancer in the US - Provenge is a kind of cell therapy that can be likened to a therapeutic vaccine, the first one to get approval in the US. Encouraging results were also obtained for ZymoGenetics' IL-21 in advanced melanoma.

Innate still has a lot of groundwork to cover but we are even more motivated to continue down this path thanks to renewed interest in our approach. It is important to remember that our approach is wholly innovative since Innate Pharma holds a pioneering and dominant position in targeting innate immunity checkpoints.

## I<sup>2</sup>: Roundtable “Immunotherapy: Pushing the boundaries in oncology”



### Discover on line the roundtable organized in Marseilles, France (in French only)

To celebrate the 10th anniversary of Innate Pharma and Ipsogen, opinion leaders in economics, research and oncology, as well as directors from biotech and pharmaceutical companies, all got together to share and compared their views on new therapeutic options and industrial developments in the French biotech pipeline.

Three roundtables on the following subjects were organised in the amphitheatre of the Centre d'Immunologie Marseille-Luminy:

- Molecular diagnosis of cancer: Customised treatments for everyone?
- Immunotherapy: Pushing the boundaries in oncology
- Back to the future of the French biotech industry: Is success just around the corner?

Each subject will be covered on the web. You can already check out the round table on immunotherapy at the following address :

[www.atcg-partners.com/table rondes/immunotherapie.html](http://www.atcg-partners.com/table rondes/immunotherapie.html)

Roundtable « Immunotherapy: Pushing the boundaries in oncology »

Moderated by Jean-Yves NAU, medical and scientific columnist at Slate.fr.

Speakers:

- **Jean-François ROSSI**, Head of Department, Hematology and Medical Oncology, CHU Saint-Eloi, Montpellier, France
- **Norbert VEY**, Onco-hematologist. Coordinator of the program Leukemia/Myelodysplastic diseases at the Institut Paoli-Calmettes, France
- **Jean-Pierre BIZZARI**, Vice-President, Clinical Oncology/Hematology, Celgene Corporation
- **Eric VIVIER**, Director of the Centre d'Immunologie de Marseille Luminy («CIML») and cofounder of Innate Pharma
- **Jean-Marc LIMACHER**, Director Medical and Regulatory Affairs, Transgene
- **Hervé BRAILLY**, CEO and cofounder of Innate Pharma

